UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,433	11/16/2001	Kristina Broliden	TRIPEP.019CP1	4011

20995 7590 02/25/2003

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER
LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
1648	10

DATE MAILED: 02/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,433	BROLIDEN ET AL.	
	Examin r	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on th cover sh et with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *9-17 and 26-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,18-25 and 34-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 1-43 are pending in the application. Claims 1-8, 18-25, and 34-43 are under consideration.

Election/Restrictions

2. Applicant's election without traverse of Group I, and of subgroup (a)(wherein the capsid agent comprises the sequence glutamine-glutamine-tyrosine, hereinafter QQY), and species (1) in Paper No. 9 is acknowledged.

3. Claims 9-17, and 26-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.

Information Disclosure Statement

4. It is noted that copy provided of reference 21 of the IDS filed on August 27, 2002, includes only pages 1 and 2 of the reference, the introduction. The reference has been considered only the extent of the material contained in that portion of the reference provided.

5. Reference 19 of the IDS filed on August 27, 2002 is identified as a PCT publication with an English abstract. As the reference is in a foreign language, and no other translation of the reference has been provided, the reference has been considered only to the extent of the contents of the abstract in the English language.

Drawings

6. New corrected drawings are required in this application for the reasons indicated on the attached Form PTO 948. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Priority

7. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Sweden on November 24, 1998. It is noted, however, that applicant has not filed a certified copy of that application as required by 35 U.S.C. 119(b).

Specification

8. The disclosure is objected to because of the following informalities: On page 25-27, the disclosure refers to Figures A-H, each showing a graph of cell growth inhibition by different pools of VP2 peptides. The various pools in the figures are referred to as pools I-VIII. However, in identifying the peptides on pages 26 to 27, the specification refers to pools 1-8. It is assumed that pool I of figure 8A comprises the peptides of pool 1 of page 26, with the remaining pools matched accordingly, but clarification of such by using the same numeric identification is requested.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-8, 18-25, and 34-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on methods of inhibiting hematopoietic cell growth by contacting the cells with a parvovirus B19 capsid agent. It is unclear from the claims what is meant by "cell growth." Alone, language would be read as the inhibition of a cell's increase in size or maturity. However, the dependant claims in indicate that another meaning is intended. See e.g., claim 24, indicating that the inhibition of cell proliferation, rather than of individual cell growth, is the purpose of the claimed method. Clarification is required.

11. Claims 1-4, 7, 8, 18, -21, 24, 25, 35-37, 39-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims all describe parvovirus VP2 capsid. Claims 4 and 5 describe a fragment of this capsid comprising a sequence of three amino acids. From claims 4 and 5 it would appear that the term "parvovirus VP2 capsid" is not actually a capsid, but the VP2 protein which is one of the constituents of the parvovirus capsid. However, it is also stated in the specification that the VP2 proteins can form a capsid in the absence of the

VP1 protein. It is therefore unclear whether the term VP2 capsid is intended to read on an individual VP2 protein, or if it is intended to represent a capsid particle comprising of only VP2 capsid subunits.

12. Claims 1-8, 18-25, and 34-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on a method of inhibiting the growth of hematopoietic cell comprising a step of "measuring the inhibition of growth of said hematopoietic cells." It is unclear why this step has been included in the claimed method. The measurement of the inhibition of growth is not a step involved in the process of inhibiting cell growth.

13. Claims 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on a method of inhibiting the growth of hematopoietic cell comprising a step of measuring the inhibition of hematopoietic cell growth wherein this measurement comprises, respectively, observing a reduction in the presence of a hematopoietic cell or observing a reduction in red blood cell hematocrit. These claims are indefinite because it is not clear what the reduction in hematocrit or in hematopoietic cells is in reference to. The methods could be measuring a reduction in cell size or number.

Further, the fact that the claimed method is to a method of reducing cell proliferation, not of killing cells renders that claim further indefinite as there is no expectation that the number or

size of the cells present in a given population would be reduced by the method. Rather, the method is intended only to prevent an increase in the number of cells presence. However, a comparative reduction in the number of cells present in a cell population may be observed between a population of cells to which the VP2 capsid has not been administered and a population to which the protein has been introduced. Thus, these claims are indefinite as it is not clear what is being measured, and as the basis for determining if there has been a reduction in cell presence is not defined.

14. Claims 37 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on methods of inhibiting the growth of hematopoietic cells by administering capsid agents comprising the sequence QQY, and wherein the capsid agent comprises a sequence from the group of SEQ ID NOs: 2-8, 45, and 48. The claim is indefinite due to the presence of the option for selecting SEQ ID NO: 45. In the absence of this option, the claim would have been interpreted as limiting the claimed method to embodiments wherein the fragment comprising QQY is, or comprises, one of the identified sequences. However, because the claims offers SEQ ID NO: 45 as an option, and this sequence does not contain the trimer QQY, the claim appears to read on a capsid agent that comprises both the QQY sequence, and one of the other identified sequences- which in the case of all SEQ ID Nos other than 45, would mean the double inclusion of the QQY sequence. It is therefore unclear if the claims are intended to read as such, or if the inclusion of SEQ ID NO: 45 was an error.

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 1, 2, 4, 7, 8, 18, 19, 21, 24, and 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims read on hematopoietic cell growth inhibiting fragments of the VP2 capsid that are at least 3 amino acids in length. However, the specification does not provide sufficient descriptive support for a claim to a genus of trimer peptides with the claimed function.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found

where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed. Such support is not present in the current application. The applicant has disclosed only a single VP2 trimer that is effective in inhibiting the growth of hematopoietic cells. While the applicant does disclose other VP2 fragments that may have such activity, none of these other fragments have as few as 3 amino acids. App., pages, 26-27. Thus, the specification does not provide sufficient written description support for a claim to any VP2 trimer capable of inhibiting hematopoietic cell growth.

17. Claims 1-8, 18-25, and 34-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of inhibiting the growth of hematopoietic cells by administering to a subject a B19 parvovirus VP2 capsid, or certain fragments thereof, does not reasonably provide enablement for using any fragment of the VP2 capsid to treat a subject for any hematopoietic disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. This rejection has two parts. First, the applicant is not enabled for the use of any fragment of the VP2 capsid that is at least three amino acids in length.

Although the applicant has shown that one VP2 peptide that is at least 3 peptides in length, the applicant has enabled one skilled in the art to practice the invention using any VP2 trimer. The only trimer that the application discloses as effective in inhibiting cell growth is the QQY fragment. No other trimers have been identified or suggested. Because the applicant has not provided any other guidance indicating that any trimer other than QQY would be capable of

performing the claimed function, the applicant is not enabled for a method of inhibiting cell growth using any such VP2 fragment.

It is noted that the application does discloses that peptides of each of the eight "pools" discussed on pages 25-27 of the application had "some degree of inhibition of colony formation" in vitro. However, the specification does not disclose that all of the tested peptides are capable of doing so. Further, by indicating that only the peptides of pool six showed "significant" cell growth inhibition, the applicant seems to be suggesting that the peptides of the other pools do not show great efficacy. If these peptides are not very operative in vitro, then more information is required to show that these peptides would be effective at all in vivo, where the peptides would be subjected to more unpredictable and harsh circumstances. This is particularly important as the only pool of peptides for which an operative region has been identified is in pool six (with the QQY trimer). While the applicant has stated that the other pools of peptides may inhibit cell growth to some extent, the applicant has not shown which peptides, or combination of peptides, from these other pools are likely to be effective.

The second reason for rejecting these claims as exceeding the scope of enablement is that the claims as written include methods of inhibiting cell growth in cancerous cell populations. See e.g., claim 25 (indicating that the method would be effective in the treatment of Polycythemia Vera, a hyperproliferative blood disorder). The art has recognized that there are issues involved in delivery of medicaments to tumor or cancer cells that do not arise in the context of other cell populations. See e.g., Jain et al, Science 271:1079-1080, and Jain et al., Cancer Metastasis Rev., 9(3): 253-266. The second of these two articles indicates that due to these problems, a showing of an in vitro efficacy is not necessarily indicative of an in vivo ability to treat cancers. Id., at

263-64. Thus, although the present application does show that the claimed methods would be operative in reducing in vitro cell proliferation, and may be useful in preventing some non-cancer or tumor related cell growth in vivo, the specification does not show that the claimed peptides or capsid agents would be effective in an anti-cancer therapy.

Conclusion

18. No claims are allowed.

19. The following prior art references are of record and are considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> Brown et al., Science, 262:114-117. This reference teaches that the B19 capsid proteins can cause the agglutination of erythrocytes expressing the P antigen. However, the reference does not teach that the capsid agent would be effective in inhibiting cell proliferation or treating a hyperproliferative disease.
>
> Mortimer et al., Nature 302: 426 and 428.This reference indicates the B19 virus can inhibit hematopoietic cell proliferation. However, the reference does not identify what portion of the virus achieves this effect. Further, the reference indicates that the virus may have this effect due to its cytotoxicity to the bone marrow cells, thus indicating that the viral infection causing cell death, rather then mere binding of the capsid to the cell, causes the inhibition. As such, the reference does not teach the use of recombinant cell capsids alone to inhibit cell growth.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
February 19, 2003

JAMES HOUSEL 2/23/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600